

# Good prognosis, clinical features, and circumstances of peanut and tree nut reactions in children treated by a specialist allergy center

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**Background:** The diagnosis of nut allergy causes anxiety. Few studies exist that estimate risk of reactions and inform management.

**Objective:** To describe frequency and circumstances of reactions after the institution of a management plan.

**Methods:** Prospective study of children with peanut/nut allergy with an allergist's management plan. Severity and circumstances of worst reaction before diagnosis (index) and follow-up reactions were evaluated.

**Results:** A total of 785 children were followed for 3640 patient-years from diagnosis. Index reactions were mild in 66% (516), moderate in 29% (224), and severe in 5% (45). Fourteen percent (114/785) had follow-up reactions (3% annual incidence rate). Ninety percent had the same/reduced severity grade, and 1 of 785 (0.1%) had a severe reaction. Preschool children ( $n = 263$ ) had a low incidence of reactions, and none were severe. There was a 3-fold reduction in injected epinephrine use from that used in the index reaction, required in 1 severe reaction, never twice; 14% (16/114) required no medication, 78% only oral antihistamines. Forty-eight percent reacted to the index nut type, 19% to a different nut (55% sensitized at diagnosis, 14% not sensitized, 31% not tested). Accidental versus index reactions were 4-fold more likely to be a result of contact exposure rather than ingestion. Contact reactions were always mild. Most (53%) reactions occurred at home, 5% in school, 21% at other sites (21% not recorded). The nut was given by a parent/self in 69 (61%) reactions or teacher in 5 (4%).

**Conclusion:** With a comprehensive management plan, accidental reactions were uncommon and usually mild, most requiring little treatment; 99.8% self-treated appropriately and 100% effectively. (*J Allergy Clin Immunol* 2008;122:286-9.)

**Key words:** Allergy, anaphylaxis, peanut, nut, management, epinephrine

Peanut and nut allergies are increasingly common,<sup>1,2</sup> and the possibility of severe/life-threatening reactions causes great anxiety among families, teachers, and medical staff alike.<sup>3,4</sup> Peanut and nut allergy are usually persistent,<sup>5</sup> and disease-modifying interventions are not available, so children have continual fear of anaphylaxis, reducing their quality of life.<sup>4</sup>

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*Abbreviation used*  
SPT: Skin prick test

Previous studies showed that children with nut allergy, despite diagnosis, continue to have frequent further reactions that apparently become more severe over time.<sup>6-8</sup> However, there are few data on the prognosis for children with nut allergy treated in allergy centers that routinely provide a comprehensive management plan.<sup>9</sup> These management plans have a positive effect on parental knowledge of avoidance measures and emergency treatment of reactions.<sup>10,11</sup> It is our experience after inception of a management plan that accidental reactions are uncommon and further severe reactions are rare.<sup>10,12</sup>

We aimed to show the annual incidence rate, severity, and risk factors for follow-up reactions in an unselected series of children with nut allergy managed by an allergy center. We extended the findings of previous studies by including subjects with both peanut and tree nut allergy. We also assessed the risks of contact exposure and reactions to other nuts, circumstances of reactions, and severity in young children. The need for and use of injectable epinephrine was identified. This information identifies the prognosis for children managed by an allergy clinic that uses a model of good practice and identifies pitfalls in food allergen avoidance, thereby improving the quality of advice provided.

## METHODS

Subjects were unselected children with peanut/nut allergy who attended the Allergy Centre in Addenbrooke's Hospital, Cambridge. Eighty percent of subjects had been referred by their primary care physicians. Diagnosis was made after a recent history of a typical type 1 hypersensitivity reaction (urticaria/angioedema  $\pm$  wheeze  $\pm$  vomiting  $\pm$  abdominal pain with change in behavior) occurring within 1 hour of definite nut ingestion together with evidence of sensitization to nuts (usually by skin prick test [SPT] wheal diameter  $\geq 3$  mm; extract from ALK-Abelló, Madrid, Spain, for peanut, almond, and hazelnut; prick-prick with fresh walnut or in house extract for Brazil, cashew, pistachio, or macadamia nut). In-house extracts were prepared as previously described.<sup>13</sup> The amount of nut, circumstances (who gave the nut, where it happened), clinical features, and treatment required for each subject's worst reaction to date (index reaction) were recorded. Severity of the index reaction was graded according to a previously published scoring system<sup>10,12</sup> (Table I). A full history of other allergic diseases was also recorded.

Each subject was enrolled in our comprehensive food allergy management package, which included the following:

- Detailed written and verbal advice on nut avoidance. We provide age-appropriate avoidance advice and routinely advise avoidance of all nut types after diagnosis.
- Provision of emergency medication selected according to previously published criteria<sup>10,12</sup> (oral antihistamines  $\pm$  intramuscular epinephrine). In the early part of the study, inhaled epinephrine was also included (until this product was withdrawn in the United Kingdom).

**TABLE I.** Clinical features of reactions in each severity grade<sup>10,12</sup>

Reaction grade	Clinical features
Mild (1-3)	1. Cutaneous urticaria/angioedema 2. Gastrointestinal symptoms 3. Rhinoconjunctivitis
Moderate (4)	Mild laryngeal edema/mild asthma
Severe (5)	Severe dyspnea/collapse

- Training of family members in the use of emergency medication, with trainer pens and a written treatment plan detailing when during a reaction the medication should be administered.
- Notification of each child's school or nursery of the diagnosis. Schools then receive a training package incorporating similar avoidance advice and emergency medication training, coordinated by local community pediatric nurses who are themselves trained in allergy. Emergency treatment plans are provided for schools.

Criteria for selection of emergency medication were based on severity of index reaction, presence of asthma, and amount of allergen ingested.<sup>10,12</sup> All patients carried oral antihistamines. Injectable epinephrine was given to those with moderate or severe index reactions and mild reactions with ongoing asthma or if only a small quantity of allergen was responsible. A small number of children with index reaction symptoms of only lip or tongue swelling were also provided with inhaled epinephrine for local application in the mouth. This was not intended as a treatment for anaphylaxis, and subjects were told not to rely on it for treatment of symptoms of airway narrowing or hypotension.

Children were followed up at intervals of 1 to 2 years, where the advice was repeated; at these appointments, information regarding accidental reactions (follow-up reactions) was recorded anonymously: the amount of nut, circumstances, clinical features, severity (graded), and treatment required.

## RESULTS

### Subject characteristics

Clinical details of 785 children with peanut and/or nut allergy with median age 68 months (interquartile range, 40-107) were collected over 3640 patient years (mean, 5.3 years; median, 4.0 years); 163 further children who were originally enrolled and characterized had no follow-up. There was no significant difference between median age, sex, nut type causing worst reaction before diagnosis (index reaction), and severity grade of index reaction for groups with or without follow-up. The prevalence of asthma in the follow-up group was 55% (434/785), and eczema, 62% (486/785).

### Index reactions

Of 785 subjects for whom details of the index reaction were available, 545 (69%) had an index reaction to peanut; 99 (13%) to Brazil nut; 42 (5%) to cashew nut; 72 (9%) to almond, walnut, or hazelnut; and 27 (4%) to others (eg, pistachio, pecan). Index reactions were mild (grade 1-3) in 66% (516/785), moderate (grade 4) in 28% (224), and severe (grade 5) in 6% (45). No treatment was required for reactions in 229 of 640 (36%), 375 (59%) had oral antihistamines only, and 36 (5%) had intramuscular epinephrine (no information in 145).

### Follow-up reactions

Of 785 subjects who were followed up, 114 had an accidental reaction over a median of 48 months of follow-up, giving an annual incidence rate of 3.1% (95% CI, 2.5% to 3.7%) for accidental reactions to all nuts. When accidental reactions caused

**TABLE II.** Number (and percentage) of follow-up reactions according to the type of nut causing the index reaction (n = 785)

Nut type causing index reaction	Index reactions (n)	No. (%) with follow-up reaction	Follow-up duration (mo), median*
Peanut	545	91 (17)	50
Brazil	99	14 (14)	50
Almond	72	9 (13)	61
Hazelnut			
Walnut			
Cashew	42	0	35

Twenty-seven subjects who had index reactions to "mixed other nut types" are not included here.

\**P* > .05 for difference between median follow-up durations.

by contact were excluded, the annual incidence rate for ingestion reactions alone was 2.0%. Numbers (and percentages) of children who had follow-up reactions in each age group were as follows: 0 to 3 years, 13 (11%); 4 to 10 years, 64 (56%); 11 to 15 years, 18 (16%); and >15 years, 19 (17%).

Follow-up reactions were caused by the same nut type that was responsible for the index reaction in 48% (55), a different type in 19% (22), and an unknown type of nut in 33% (37). Of those who reacted to a different nut type, 55% (12) were sensitized to that nut at enrollment, 14% (3) were not, and 31% (7) were not tested. There was no relationship between the size of SPT wheal for the index nut and the risk of accidental reactions (data not shown).

### Nut type and subsequent risk

There was no association between the nut type that caused the original reactions and the odds of having a follow-up reaction, with the exception that follow-up reactions were not seen to cashew nut (Table II).

### Circumstances of follow-up reactions

The majority of accidental reactions were caused by the parents or children themselves, and most follow-up reactions occurred at home (Table III). Very few reactions occurred at school or were caused by teachers. A significant proportion of reactions occurred during organized activities outside the home.

### Severity

Overall, for follow-up reactions, 81% (92/114) were mild (grade 1-3), 18% (21) moderate (grade 4), and 1% (1) severe (grade 5). All reactions caused by cutaneous contact were mild (n = 40). For ingestion, 52 of 74 (70%) reactions were mild and 22 (30%) moderate-severe. No follow-up reactions were caused by inhalation of peanut protein. Compared with the severity of the index reactions for each child, 64% of follow-up reactions were of the same severity grade, 26% were of a lower grade, and 10% were of a higher grade (n = 114). For those with a higher severity grade, 10 of 11 changed from mild to moderate and 1 of 11 from moderate to severe; 1 required no treatment, 9 received oral antihistamine, and 1 child with a severe reaction received intramuscular epinephrine appropriately as per the treatment plan.

### Medication

Overall, for follow-up reactions, 16 of 114 (14%) required no treatment, 89 (78%) had oral antihistamines only, 6 (5%) had

**TABLE III.** Circumstances of follow-up reactions (n = 114)

Site of follow-up reaction	No. (%)	Who gave the nut that caused the follow-up reaction?	No. (%)
Home	60 (53)	Parent	47 (41)
School	6 (5)	Self	22 (19)
Party	14 (12)	Teacher	5 (4)
Other*	10 (9)	Waiter	5 (4)
Unknown	24 (21)	Other†	10 (9)
		Unknown	25 (23)

\*Includes restaurant, airplane, Santa's grotto, church, scout hut.

†Includes Father Christmas, scout master, aircraft cabin crew, friends.

inhaled epinephrine, and 3 (3%) had a single intramuscular epinephrine injection (used for severity grades mild, moderate, and severe, 1 each). All were treated by using medication from the emergency treatment plan. We also compared the medication used during the index reaction with that used in the follow-up reaction for 112 subjects for whom complete data were available. Compared with index reactions, there was a 3-fold reduction in injected epinephrine use (Table IV).

## DISCUSSION

We have shown a favorable prognosis for children attending a specialist allergy clinic with an annual incidence rate for accidental ingestion of peanut and/or tree nuts after diagnosis of 3%.

This rate is substantially lower than rates in other studies of accidental exposure to peanut alone. For example, in 1989, Bock and Atkins<sup>8</sup> found 50% of children with peanut allergy had an accidental ingestion within the past year. Vander Leek et al<sup>14</sup> found an annual incidence rate of 33%, and most recently, Yu et al<sup>7</sup> reported a rate of 14%. Another study found a follow-up reaction rate for peanut and tree nut allergy of 55% over a period of 5.4 years.<sup>15</sup> However, it is not explicit whether management plans were in place for all subjects, although the diagnosis had been made. In an earlier follow-up study of the effect of a comprehensive management plan, we found an annual incidence rate of 6% (and an 8-fold reduction in reaction frequency before and after the introduction of a plan).<sup>10</sup> We suggest that the comprehensive introduction of a consistent, structured management plan for all our subjects, detailing family, school, and medical education, is responsible for the observed low rate of reactions. Other factors include improved food industry guidance on food labeling and allergen avoidance as well as public awareness.

There is evidence that peanut allergy is presenting at a younger age than previously.<sup>16</sup> Two thirds of children in the current study had onset of allergy in the preschool years (<4 years). The diagnosis of this potentially severe allergy in preschool children causes great anxiety for families. However, our data are reassuring. Only 11% of follow-up reactions occurred in this age group. The majority (12/13; 92%) were mild and 1 moderate (mild laryngeal edema), and all 13 reactions were treated with oral antihistamines alone.

We are frequently asked about the consequences of accidental skin contact reactions in a child with known peanut or nut allergy. Severe reactions to cutaneous contact have been described,<sup>17</sup> although more recent data are reassuring—for example, peanut butter causing only local reactions, and no respiratory or systemic reactions after inhalation.<sup>18,19</sup> Our data provide further reassurance because all accidental skin contact reactions were mild. In cases in which follow-up reactions were caused by ingestion, 30% of reactions involved at least some degree of reported airway

**TABLE IV.** Medication used for index and follow-up reactions in 112 subjects for whom data are available for both follow-up and index reactions (data were available for 112 index and 114 follow-up reactions)

	Index reaction	Follow-up reaction
No treatment	42 (38)	16 (14)
Oral antihistamines only	61 (54)	87 (78)
Inhaled epinephrine	0	6 (5)
Intramuscular epinephrine	9 (8)†	3 (3)*†

No. (%).

\*One inappropriate use.

†Difference between proportions is 0.06; 95% CIs, -0.005 to +0.125.

narrowing. Avoidance advice should therefore be concentrated on measures to reduce ingestion of nut.

This is the first study that describes whether children reacted to the same or a different nut type during worst initial and accidental reactions. Despite our advice to avoid all nut types, at least 1/5 reacted to a different one, not previously ingested, and at least half of those were known to have a positive SPT to that type at presentation.

The decision of whether to advise children to avoid all nuts or only the one causing the index reaction should include the following considerations. Children with nut allergy have a poor ability to distinguish different nut types on the basis of appearance.<sup>20</sup> Further, peanut is commonly used by manufacturers to bulk out other nut types in foods in which the nut type cannot be clearly identified, such as sauces. In 2-year-olds with peanut allergy, 19% are sensitized to at least 2 nut types, rising with age to 73% at 10 years.<sup>21</sup> Our data show that at least 19% reacted to a different nut from the index nut at follow-up, of which a significant proportion of reactions were potentially avoidable. In schools, the only workable policy is no nuts rather than each child avoiding a different nut. The majority of accidental reactions happened in school-age children (56%), but very few occurred on school premises (5%), with the majority arising at home (53%). The person responsible for supplying the nut was most often a parent (41%), the child (19%), or uncommonly, a teacher (4%). This is contrary to the findings of some previous studies,<sup>22,23</sup> except a recent Canadian series that also found a low rate of accidental peanut reactions in schools.<sup>7</sup> This group partly attributed the low rate of school reactions to widely implemented avoidance procedures in Montreal schools.<sup>7</sup> In our referral population, schools are guided by close liaison with allergy-trained pediatric nurses who provide a comprehensive training package for teachers and catering staff covering allergen avoidance advice and use of emergency medication.<sup>9,12</sup> Each child with food allergy carries an emergency treatment plan.

A significant proportion of accidental reactions in school-age children occurred outside the school and home, and we found a wide range of situations and persons responsible for causing accidental reactions including parties, scout groups, aircraft, restaurants, churches, and even Father Christmas grottos. At diagnosis, families must be made aware of the need to inform anyone interacting with the child outside the home about avoidance measures.

Cashew nut allergy appears to be increasing in prevalence and was the third most common cause of index reactions in this series, whereas this was rare in the early 1990s.<sup>24</sup> A greater proportion of reactions to cashew are severe compared with peanut.<sup>13</sup> Yet there were no accidental follow-up reactions, presumably because it is

relatively easy to avoid, being less often used an ingredient or hidden in foods.

It is a widely held view that subsequent reactions to nuts may become more severe over time.<sup>6-8,14</sup> Yu et al<sup>7</sup> found that 31% of subsequent reactions to peanuts were more severe than the first, Hourihane et al<sup>6</sup> found 59% of children had more severe recent than first reaction, and Vander Leek et al<sup>14</sup> found 44% of children with an initial "non-life-threatening" reaction to peanut had a subsequent "potentially life-threatening" reaction. Subjects in the study by Yu et al<sup>7</sup> were enrolled in a management plan; it is not clear whether this was the case in the other studies.<sup>6,14</sup> These studies comparing the first and subsequent reactions suggest they appear to increase in severity with time. This might be influenced by the amount of nut ingested rather than an intrinsic worsening of the disease. In contrast, our study compares the worst reaction before intervention with subsequent reactions. The evidence is that with a comprehensive management plan, the new development of severe reactions is rare (0.1%). With our management plan, most reactions after inadvertent ingestion are to smaller amounts, and hence, severity is reduced.<sup>10,12</sup> We have previously shown a relationship between the amount of nut exposure and severity of reaction.<sup>12</sup> In cases in which severity did increase (from mild to moderate), this was usually not clinically significant: although 10% (11/114) had follow-up reactions in a higher severity group than the index reaction, 10 of 11 (91%) required either no treatment or oral antihistamines alone.

Our sample consisted of allergy clinic attendees. We believe that this sample is broadly representative of children with peanut and nut allergy, because 80% of referrals were made by primary care physicians from a large geographical area. We are the only allergy service in this area. It may be argued, however, that a small group of children with mild allergy may not have been referred.

In summary, we have shown that under the care of a specialist allergy center, the prognosis for children with nut allergy is good, with a low frequency and severity of further reactions, especially among preschool children, and overall there is an infrequent need for injected epinephrine. Interventions such as oral desensitization are being developed to prevent accidental reactions; however, until they are available, we should learn from these reactions how to improve allergen avoidance advice.<sup>25</sup> We have highlighted that school age children are most at risk and that reactions occur most commonly at home, but also commonly outside the home and school. With informed school training by professionals with expertise, few reactions occurred in school. Families and schools can be reassured that contact reactions were always mild. Children who present with nut allergy should have specific IgE testing to the common nut types, and avoidance of other nut types should be considered, according to individual circumstances.

**Clinical implications: The prognosis with specialist care is good. Preschool children have low incidence of reactions, which are mild. Accidental reactions occur to other nut types and commonly outside the home and school.**

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